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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/996,114	11/28/2001	Gergely M. Makara	111025.152	1583
26161	7590	08/06/2004	EXAMINER	
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			CLOW, LORI A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 08/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9M.

<b>Office Action Summary</b>	<b>Application No.</b> 09/996,114	<b>Applicant(s)</b> MAKARA, GERGELY M.	
	<b>Examiner</b> Lori A. Clow, Ph.D.	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 November 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 22, 23 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-21, 24 and 26-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |  |
|--|--|
| <p>1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)</p> <p>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</p> <p>3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br/>Paper No(s)/Mail Date <u>10/07 and 9/30/02</u>.</p> | <p>4) <input type="checkbox"/> Interview Summary (PTO-413)<br/>Paper No(s)/Mail Date. _____</p> <p>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</p> <p>6) <input type="checkbox"/> Other: _____</p> |
|--|--|

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### **DETAILED ACTION**

Applicant's election without traverse of Claims 1-21, 24, and 26-28 and Species B in the reply filed on 24 November 2003 is acknowledged.

Claims 22, 23, and 25 are hereby withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

### **Specification**

The Specification is objected to for reciting at page 1, line 1, "this application claims priority from". The sentence should read "this application claims the benefit of". Appropriate correction is requested.

### **Information Disclosure Statement**

The information disclosure statements (IDS) submitted on 30 September 2002 and 7 October 2002 have been considered. Signed copies of PTO forms 1449 are included with this Office Action.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21, 24, and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the **claimed** invention one of skill in the art must be able to characterize a molecule for determining molecular similarity or diversity. For the reasons discussed below, this constitutes undue experimentation.

b) The specification provides examples for capturing shape by calculating pairwise distances between heavy atoms and generating a curve which sorts distances by increasing or decreasing order to create a fingerprint. A weighting approach, based on molecule size and the number of occurrences of properties, is then used to somehow yield similarity values (pages 10-16). The claims, however, provide no steps such that a similarity or a diversity is actually determined. The claims determine distances of atoms to somehow characterize shape, without any step of comparison of distances to determine a shape according to the method of the specification. At the next step, a group of properties, which are neither defined nor derived, are associated with atoms. Further, the claims comprise sorting distances by magnitude to create a curve. Again, the claims do not recite if the curve is a curve of increasing similarity or diversity or decreasing similarity or diversity. One of skill in the art would not know how to generate the curve or use the curve practicing the recited method. Further, the curve is then numerically

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characterized. However, how is it characterized? What does the curve mean? Lastly, values are stored. Again, there is no step of characterizing a molecule for determining molecular similarity or diversity in the recited methods.

c) The specification provides no working examples of the instant method.

d) The invention is drawn to characterizing a molecule for determining a molecular similarity or diversity.

e) It would have been well known in the art that pharmacophore diversity is evaluated by several well-known methods, such as CoMFA, CoMMA, QSAR, and QSCD. While each method defines a slightly different approach for molecular comparison, compounds of the same pharmacological class can be identified as being similar or different. For example, in COMFA (comparative molecular field analysis) structure/activity relationships can be determined. It is based upon 1) representation of ligand molecules by their steric and electrostatic fields, sampled at the intersections of a three-dimensional lattice; 2) a “fit field” technique, allowing alignment within a series, by minimizing the RMS field differences between molecules; 3) data analysis by partial least squares, using cross validation to maximize the likelihood that the results have predictive validity; and 4) graphic representation of the results. The detailed steps of this method predict relationships among molecules using data tables, whose columns are numerical property values and whose rows are compounds, usually taking the form of a linear equation. It is clear that in this method the representation of data, by a table, is clearly defined such that relationships are established. The rows and columns are defined. Unlike the curve of the instant claimed invention, numerical representations of properties are defined in a specific manner (see J.

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American Chem. Society (1988) Vol. 110, pages 5959-5967 for a complete description of CoMFA).

f) The skill of those in the art of pharmacophore analysis is high.

g) The prior art indicates that molecular diversity and similarity calculations are made by various specific techniques which include steps of comparison so as to generate a meaningful similarity or diversity.

h) The claims are broad because they are drawn to determining distance between atoms and properties without characterizing either the property or the distance such that it generates a similarity or diversity.

The skilled practitioner would first turn to the instant specification for guidance to practice methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that such methods are highly specific and require specific steps in which to generate a similarity or diversity, absent in the instant claimed methods. Finally, said practitioner would turn to trial and error experimentation to determine whether the steps of the claimed methods generate a similarity. Such represents undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-21, 24, and 26-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 26, and 27 recites a method of characterizing a molecule for determining molecular similarity or diversity. However, no such step of determining similarity or diversity is present. Clarification is requested.

Claim 1 recites a first step of determining intermolecular distances between atoms and a second step that incorporates properties. However, it is unclear how step 1 relates to step 2. From where do the properties come? Do the properties relate to the individual atoms or the overall molecule? Clarification is requested.

Claim 2 recites “sorting distance by magnitude”. Is the sorting done in terms of increasing or decreasing magnitude or both. Clarification is requested.

Claims 18 and 21 recites “the method further comprising searching the fingerprints in the database to identify a molecule that has the desired shape and/or properties”. It is unclear what this step has to do with the determination that a molecule is desired. Is the desired molecule compared to other fingerprints in a database? Clarification is requested.

Claim 24 recites “sufficiently similar”. The metes and bounds of “sufficiently” are not defined such that one of skill in the art could determine its meaning in the context of the claim. Is something sufficiently similar if they are close in distance, if the properties of the atoms are the same etc...? Clarification is requested.

Claim 26 recites “sorting distances”. Is the sorting done in terms of increasing or decreasing magnitude or both. Clarification is requested.

No claims are allowed.

### **Inquiries**

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Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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August 4, 2004  
Lori A. Clow, Ph.D.  
Art Unit 1631

*Lori A. Clow*

MARJORIE MORAN  
PATENT EXAMINER

*Marjorie A. Moran*  
8/5/04